DETECTION OF STROKE DURING CARDIAC OPERATIONS WITH SOMATOSENSORY EVOKED RESPONSES

Mark M. Stecker, MD, PhD[a]
Albert T. Cheung, MD[b]
Terry Patterson, PhD[a]
Joseph S. Savino, MD[b]
Stuart J. Weiss, MD, PhD[b]
Rafael M. Richards, MS[b]
Joseph E. Bavaria, MD[c]
Timothy J. Gardner, MD[c]

Objectives: **The objectives of this study were to determine if monitoring of intraoperative somatosensory evoked potentials could be used to detect stroke during cardiac operations and to establish indicators of cerebral ischemia based on changes in these potentials.** ***Methods:*** **Twenty-five patients undergoing cardiac operations underwent preoperative and postoperative neurologic examinations as well as intraoperative recording of somatosensory evoked potentials. Detailed analysis of the waveforms of these potentials was performed.** ***Results:*** **Two of the 25 patients had intraoperative strokes. These patients and only these patients had changes in their somatosensory evoked potentials during the operation suggesting cerebral ischemia. The unilateral disappearance of the cortical somatosensory evoked potential waves correlated significantly with the clinical outcome of stroke ($p < 0.004$). Ischemic changes were detected in real time and were related to the removal of the aortic crossclamp in one patient and to the initiation of cardiopulmonary bypass in the other.** ***Conclusions:*** **Somatosensory evoked potentials can detect intraoperative stroke during cardiac operations. Acute, unilateral decreases in amplitude of the cortical potential are more useful than changes in latency in detecting intraoperative stroke. (J Thorac Cardiovasc Surg 1996;112:962-72)**

Neurologic deficits ranging from subtle changes in cognitive function to stroke are significant causes of disability after cardiac operations.[1-3] Toward the goal of preventing neurologic injury during cardiac operations, important steps include detecting cerebral ischemia in real time and firmly establishing the pathophysiologic mechanisms and exact operative events that lead to these injuries. Although it is difficult to detect acute neurologic events in anesthetized patients, four different types of cerebral monitoring have been explored. First, cerebral arterial flow can be monitored for the presence of emboli by means of transcranial Doppler ultrasonography.[4, 5] Studies using transcranial Doppler ultrasonography have demonstrated that patients having a larger number of emboli were at greater risk for neuropsychologic complications than were patients in whom smaller numbers of emboli were detected; however, it was not possible to identify which individuals had cerebral ischemia or which embolic events contributed to neurologic injury.[4] Alternatively, biochemical measurements of creatine kinase BB isoenzyme fraction[6] or cerebrospinal fluid adenylate kinase[7] have been used as markers for brain injury but are not yet useful during operations because they cannot be measured quickly and therefore cannot identify the exact timing of neurologic injury. Other biochemical markers of cerebral ischemia such as jugular venous oxygen tension[8] may be measured in real time but are affected by factors other than cerebral ischemia. Electroencephalographic (EEG) monitoring[9-12] is a sensitive, easy to perform technique that can provide real-time results, but its interpretation is complicated by the substantial effects of temperature, anesthetics, and electrical interference, as well as the absence of unequivocal criteria[12] for "abnormality" during cardiac operations. Somatosensory evoked potential (SEP) monitoring[13-16] has been shown to be sensitive for detecting cerebral isch-

From the Departments of Anesthesiology,[b] Neurology,[a] and Surgery.[c] University of Pennsylvania, Philadelphia, Pa.

M.M.S. was supported by National Institute of Neurologic Diseases Clinical Investigator Development Award NS01502.

Received for publication March 20, 1996; revisions requested May 8, 1996; revisions received May 21, 1996; accepted for publication June 4, 1996.

Address for reprints: Mark M. Stecker, MD, PhD, Department of Neurology, Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia, PA 19104-4283.

0022-5223/96 $5.00 + 0 **12/1/75522**

emia[17] and represents an alternative to EEG monitoring because the effects of temperature and anesthetic agents on the evoked responses are predictable[18, 19] and the signal averaging inherent in the SEP method helps to reduce the effect of environmental noise. However, the sensitivity or specificity of SEP recording for detecting cerebral ischemia during cardiac operations in human beings has not been established.

The objectives of this study were to determine whether intraoperative SEP monitoring can be used to predict the occurrence of intraoperative stroke during cardiac operations in which deliberate hypothermia and cardiopulmonary bypass are used and to define the technical factors that affect the sensitivity and specificity of this monitoring technique.

Patients and methods

Subjects and neurologic examinations. With written informed consent, 25 patients undergoing elective cardiac operations that did not involve hypothermic circulatory arrest were studied in accordance with a clinical protocol approved by the University of Pennsylvania Committee on Studies Involving Human Beings (May 23, 1994). Each of these 25 patients had (1) normal results of a neurologic examination on the day before the operation, (2) a documented, formal neurologic examination at 72 to 96 hours after the operation, and (3) a technically adequate intraoperative SEP recording. Computed tomographic scans of the head were performed on patients with postoperative neurologic examinations that indicated a stroke.

Anesthesia and operations. General anesthesia was induced and maintained by the administration of fentanyl, midazolam, pancuronium, and 100% oxygen. Volatile anesthetics were not administered in 19 patients. In five patients up to 0.5% isoflurane was administered, and in one patient up to 0.5% halothane was administered. Nasopharyngeal and bladder temperatures were continuously monitored. Cardiopulmonary bypass was instituted with a circuit consisting of a centrifugal pump, membrane oxygenator (Maxima Plus, Medtronic, Inc., Anaheim, Calif.) and an in-line 35 μm arterial filter (Bard H-690, C.R. Bard, Inc., Tewksbury, Mass.). Patients were cooled to nasopharyngeal temperatures ranging from 18° to 32° C (Table I) at a rate ranging from 0.3° C/min to 1.3° C/min during cardiopulmonary bypass. After ventricular fibrillation, the ascending aorta was crossclamped and cardiopulmonary bypass was maintained at a cardiac index of 2.2 L/min per square meter and a mean arterial pressure of 65 mm Hg. Rewarming on cardiopulmonary bypass was performed at a rate of approximately 0.5° C/min.

SEPs. Bilateral upper extremity SEPs were recorded (Viking IIe or Viking IV, Nicolet Biomedical, Madison, Wis.) at 3-minute or shorter intervals throughout the entire operation. Typically 500 to 750 averages were acquired for each trace. The somatosensory stimulus consisted of 0.5 msec duration electrical pulses applied to the right and left ulnar nerves at the wrist through 3.5 × 2.0 cm surface gel electrodes (Nicolet Biomedical) at a rate of 5.7 Hz. The intensity of these pulses was 25 mA for most studies, but in eight of the 25 patients the stimulus intensity was systematically varied between 4 and 25 mA. In studies in which the Viking IV unit was used, stimulation of the right and left ulnar nerves was carried out in an interleaved fashion so that SEPs from both sides could be obtained simultaneously. In studies in which the Viking II unit was used, SEPs were obtained first from one side and then from the contralateral side in an alternating fashion so that there was a lag of approximately 3 minutes between corresponding right-sided and left-sided evoked responses. Recordings were made from electrodes placed 2 to 3 cm posterior to the right and left Erb points, the neck, and the C3′ and C4′ scalp electrode positions. Four channels were recorded (C4′-C3′, neck-Fpz, C4′–left Erb, C3′–right Erb). SEPs were recorded with an analysis time of 50 msec during normothermia, but a 100 msec analysis time was used during hypothermia because of the increased latency of the responses. The following potentials were identified according to the criteria of the American EEG Society[20]: the Erb point potential that arises from the brachial plexus, the N13 potential that arises from the cervicomedullary junction, the N18 potential that arises from the brain stem, the N20 potential arising from the thalamus and cortex, and the P22 potential arising from the somatosensory cortex. According to standard convention, the names of the various potentials are based on whether they are positive (P) or negative (N) and on the latency of the wave in normothermic normal individuals (Fig. 1, *A*). The latency of each potential, as well as the peak-to-peak amplitude of the N20-P22 complex, was also measured. All latency and amplitude data from each evoked response were entered into a database.

Large temperature- and anesthesia-related changes in the evoked potential latency and amplitude can occur during cardiac operations. For this reason, a number of secondary parameters were derived from the raw evoked potential data, with the expectation that they would show less temperature- or anesthesia-related variability and would more clearly demonstrate any effects of cerebral ischemia. For each set of evoked responses, the "amplitude asymmetry" was defined as the ratio of the amplitudes of the N20-P22 complex obtained from stimulation of the right and left arms with the larger amplitude taken as the numerator. When the value of one of the amplitudes was too small to be measured, it was arbitrarily assigned an amplitude of 0.05 μV, which is a very conservative estimate of the lowest amplitude of the N20-P22 complex detectable with our evoked potential method and equipment. Because anesthetics and temperature will affect both sides similarly, the amplitude asymmetry will be less dependent on these factors than the raw amplitude measurements. The amplitude asymmetry may be insensitive to bilateral cerebral ischemia; thus another amplitude-related parameter was studied, the "amplitude variability." For each measurement, the ratio of each patient's largest N20-P22 amplitude to the amplitude of the N20-P22 complex on that same side was computed. The largest value from either side was taken as the amplitude variability. A "latency asymmetry" was defined for the Erb

Table I. *Clinical summary data*

Patient No. (age, sex)	*Operation*	*Preop. exam*	*Postop. exam*	*SEP change*	*Lowest temp. (°C)*
1 (63, M)	CABG × 3	Normal	Decreased strength in intrinsic hand muscles on R with no upper motor neuron findings. C/W mild R lower plexopathy.	No	31.8
2 (65, M)	MVR	Normal	Normal	No	21.9
3 (63, M)	CABG redo, MVR	Normal	Normal	No	26.8
4 (73, F)	CABG × 3	Normal	Normal	No	29.8
5 (46, F)	MVR	Normal	Normal	No	30.2
6 (76, M)	CABG × 3	Normal	Normal	No	24.2
7 (70, M)	CABG × 2, AVR	Normal	Normal	No	18.7
8 (68, M)	CABG redo	Normal	Normal	No	29.6
9 (32, F)	CABG × 3 w/LITA	Normal	Normal	No	31.3
10 (68, F)	CABG × 3	Normal	Normal	No	23.7
11 (69, F)	CABG × 1	Normal	Normal	No	28.9
12 (53, M)	CABG × 2 w/LITA	Normal	Normal	No	31.5
13 (63, M)	CABG × 4	Normal	Normal	No	27.6
14 (51, M)	CABG × 4, AVR	Normal	Normal	No	28.4
15 (75, M)	CABG × 3, CEA	Normal	Normal	No	27.9
16 (75, M)	MVR redo, mitral stenosis	Normal	Initial L hemiparesis with recovery of L arm strength and persisting moderate L leg weakness.	Thirty-minute loss of N20-P22 from stimulation of L ulnar nerve. Erb,N13,N18 preserved.	23.8
17 (70, M)	CABG × 3 w/LITA	Normal	Normal	No	28.6
18 (72, F)	AVR, CABG	Normal	Mild decrease in strength in intrinsic hand muscles on R with no upper motor neuron findings. C/W mild R lower plexopathy.	No	29.4
19 (64, M)	CABG redo	Normal	Normal	No	28.7
20 (34, F)	AVR w/aortic root repair	Normal	L hemiplegia with upgoing toe and increased reflexes on L. CT→Infarct in posterior limb of R internal capsule.	Twelve-minute loss of N20-P22 from stimulation of L ulnar nerve with aortic cannulation. SEPs recovered but another 25-minute period of flattening occurred during rewarming. N13,Erb,N18 preserved.	26.8
21 (24, M)	AVR, CABG	Normal	Normal	No	22.7
22 (67, F)	CABG, MVR, CEA	Normal	Normal	No	23.9
23 (22, M)	AVR	Normal	Normal	No	29.6
24 (69, F)	CABG × 4, L CEA, R carotid occlusion	Normal	Normal	No	25.2
25 (61, M)	AVR	Normal	Normal	No	33.5

AVR, Aortic valve replacement; *CABG,* coronary artery bypass grafting; *CEA,* carotid endarterectomy; *CT,* computed tomographic scan; *C/W,* consistent with; *L,* left; *LITA,* left internal thoracic graft; *MVR,* mitral valve replacement; *R,* right.

point, N13, N20, and P22 potentials as the absolute value of the difference in latencies between corresponding potentials on the left and right.

A conservative criterion for a "significant" change in the SEP was established a priori to provide real-time feedback to the surgeons and anesthesiologists about the possibility of central nervous system ischemia. This criterion defined a significant change as an acute, unilateral disappearance of one or more waves in the SEP that persisted for more than 3 minutes and could not be attributed to the effects of a sudden change in temperature. Although this criterion was strict, the initial goal was to interpret changes in the SEPs as conservatively as possible until further guidelines could be established for

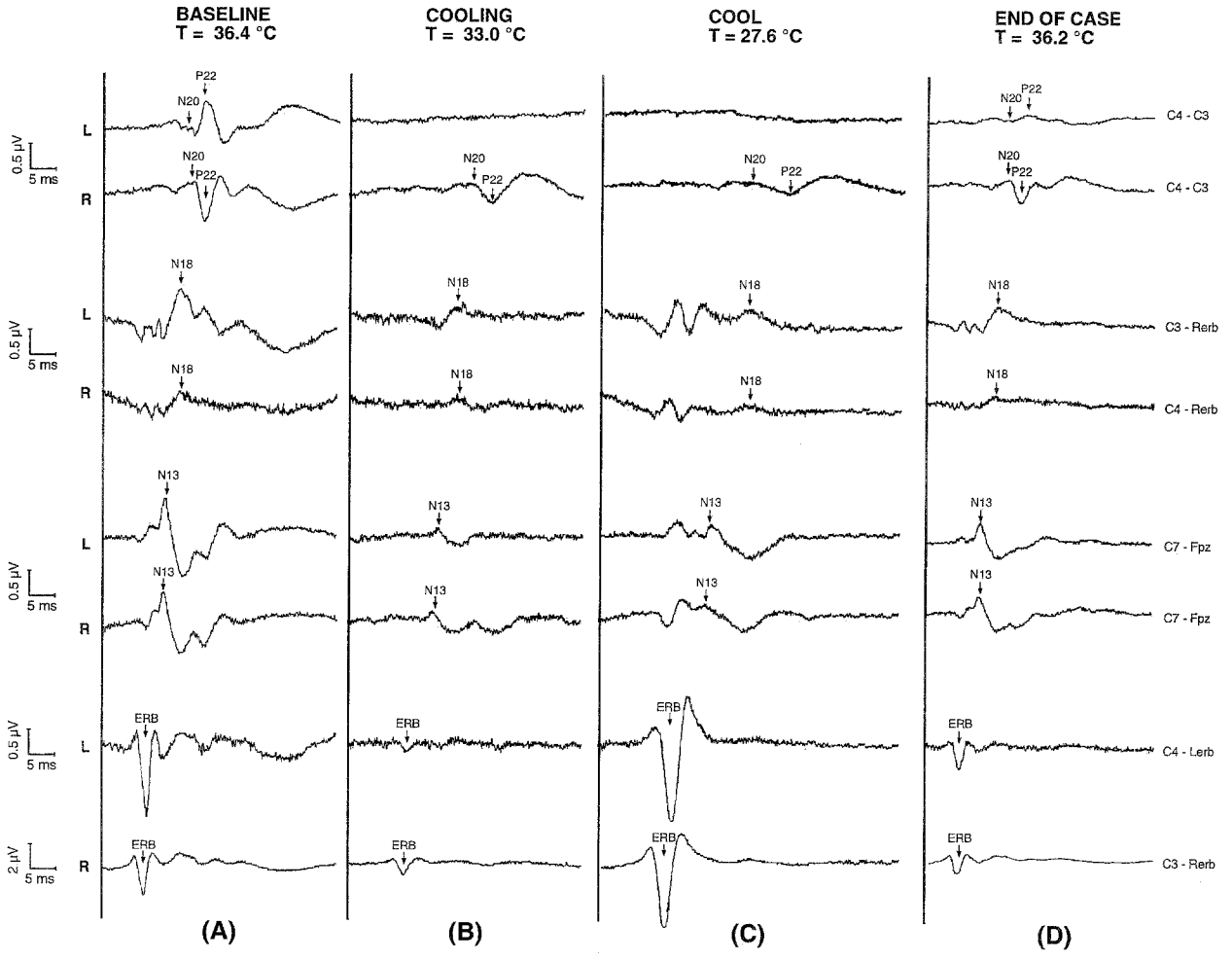

Fig. 1. A, SEP recording obtained at baseline from patient 20. This tracing demonstrates the "normal" morphology of the SEP during cardiac surgery. **B,** SEP recorded after the initiation of cardiopulmonary bypass and active cooling. In comparison with **A,** the N20-P22 complex arising from stimulation of the left arm and representing activity in the left thalamus and cortex has disappeared whereas that arising from stimulation of the right arm remains intact. There is a prolongation in the latency of the responses owing to cooling. Note that the spinal (N13) and brain stem (N18) potentials remain present bilaterally. With continued cooling **(C),** the latency of all waves increases but the N20-P22 complex from stimulation of the left arm remained absent. By the end of the operation **(D),** the amplitude of the N20-P22 complex from stimulation of the left arm has recovered somewhat, but continues to be of much lower amplitude than at the beginning of the case. In this figure, left and right refer to the ulnar nerve that was stimulated. *T,* Temperature; *Rerb,* right Erb point; *Lerb,* left Erb point.

significant changes during cardiac operations. Latency criteria were not part of our a priori criterion because of the substantial temperature-related latency changes seen during cardiac operations. The site of injury or ischemia was localized by the pattern of loss in the SEP waves. For example, the loss of the N20 and P22 waves in response to stimulation of the left arm would indicate ischemia above the level of the brain stem on the right side of the brain. The loss of the Erb point potential, as well as all subsequent potentials, would suggest a lesion between the stimulating electrodes and the brachial plexus.

Analysis of temperature effects. The temperature dependence of SEP latencies and amplitudes was analyzed by linear regression with the latency or amplitude of the waves recorded from stimulation of the left ulnar nerve as the dependent variable and the nasopharyngeal temperature as the independent variable. The process was repeated with the analogous waves produced by stimulation of the right arm. The slope and standard deviation values from the left and right sides were then averaged.

To test whether the derived measures of amplitude asymmetry or amplitude variability were affected by tem-

Table II. *Correlation of SEP change with intraoperative stroke*

	SEP change	
	Yes	*No*
Stroke		
Yes	2	0
No	0	23

perature, we performed a Spearman rank correlation analysis between each of these parameters and the nasopharyngeal temperature.

Statistical analysis. A 2 × 2 table was generated containing the number of patients with and without SEP changes according to the a priori criteria outlined earlier as a function of whether they had a stroke. The statistical significance of this table is assessed according to Fisher's exact test.

To determine what evoked potential parameters and critical values would be useful in predicting whether patients had intraoperative strokes, we determined the values of each of six parameters for each patient: (1) the maximum observed value of the amplitude asymmetry, (2) the maximum observed value of the amplitude variability, and (3-6) the maximum value of the difference in latency between the left and right Erb points, N13, N20, and P22 potentials. Each of these variables has the property that larger values (i.e., large amplitude changes or large latency differences) could be expected in patients with neurologic injury. The ability of any of these variables to classify patients according to the neurologic outcome of the operation was tested by taking the largest value of each parameter for each patient and subjecting these maximum values to a linear discriminant analysis (STATISTICA, StatSoft, Inc., Tulsa Okla.). Only the 21 patients with normal preoperative and postoperative neurologic examinations (normals subjects) and the two patients with clear intraoperative strokes were included in this analysis.

Results

Subjects and neurologic examinations. Patients' ages ranged between 22 and 78 years. Sixty-four percent of the patients were male. Coronary artery bypass grafting (CABG) alone was performed in 11 patients, valve replacement alone in six patients, combined valve replacement and CABG in five patients, and combined carotid endarterectomy and CABG or valve repair in three patients (see Table I). None of the patients undergoing carotid endarterectomy had any EEG or SEP changes during clamping of the carotid artery. Patients 15 and 22 did have shunts placed during the endarterectomy. Four of the 25 patients had abnormal results on postoperative neurologic examinations. In two of the four patients with focal neurologic deficits, the neurologic examination indicated a stroke. Patient 16, whose case was reported previously,[21] had a right frontal-periventricular infarction on follow-up computed tomographic scan and an initial left hemiparesis that improved over a few days to the point where there was only 4+/5 weakness in the left leg and 5/5 strength in the left arm. Patient 20 had an infarction in the region of the posterior limb of the right internal capsule that was verified by serial computed tomographic scans and manifested clinically as a dense left hemiparesis involving the face, arm, and leg. Light touch and vibration sensation were intact although two-point discrimination was slightly reduced on the left side. In patients 1 and 18, results of the neurologic examination indicated a mild right-sided lower brachial plexopathy.

SEP responses. SEP recordings were always interpretable when the temperature was stable. However, in seven patients, rapid cooling (average rate of 0.95° C/min) during cardiopulmonary bypass was associated with a period of less than 3 to 6 minutes during which the cortical SEP waves became difficult to detect bilaterally. As the temperature stabilized, the cortical SEPs returned despite continuing hypothermia.

The SEP recordings were interpreted during the operation in real time and then later reviewed by two of us (T.P. and M.M.S.). Each of these interpretations was in agreement.

On the basis of the a priori criterion for a significant change in the SEP outlined earlier, intraoperative SEP monitoring correctly identified, in real time, the two patients who had intraoperative cerebral ischemia, and it did not show significant changes in the 23 patients without stroke (Table II). This correlation was significant ($p < 0.004$) by Fisher's exact test.

The pattern of the SEP changes in the two patients with stroke consisted of a transient disappearance of the N20-P22 potentials on the side of the infarction with preservation of the shorter latency potentials arising from the brachial plexus, cervico-medullary junction, and brain stem. In both cases the N20-P22 potentials returned gradually toward baseline by the end of the operation. In patient 16, who had an intraoperative stroke, loss of the N20-P22 complex occurred with the removal of the aortic crossclamp and persisted for 17 minutes before recovery began. In patient 20, the second patient with an intraoperative stroke, the N20-P22 complex disappeared immediately after the initiation of cardiopulmonary bypass. The N20-P22 complex was absent for a 12-minute period and then recovered during hypothermia (Figs. 1 and 2, *B*).

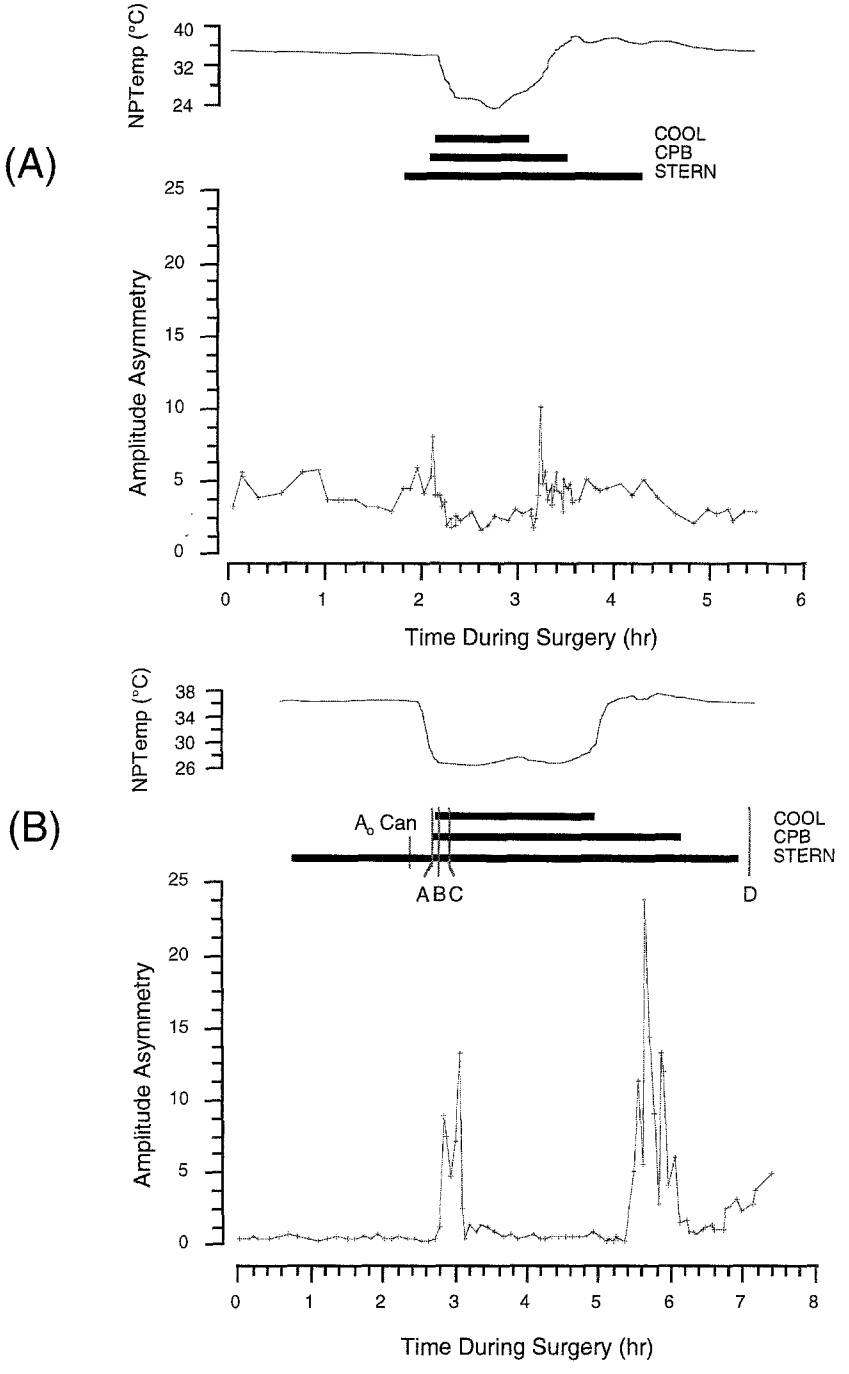

Fig. 2. A, Changes in amplitude asymmetry during the operation in patient 6, who did not have an intraoperative stroke. The largest values of the amplitude asymmetry occurred during rapid temperature changes and were of short duration. **B,** The time course of the amplitude asymmetry in patient 20, who did have an intraoperative stroke. The acute increase in amplitude asymmetry during the initiation of cardiopulmonary bypass indicates the onset of cerebral ischemia. The labels *A-D* on this figure refer to the corresponding evoked potential tracings shown in Fig. 1. *COOL,* Time of active cooling; *CPB,* time of cardiopulmonary bypass; *STERN,* time of sternotomy from opening to closure; A_o *Can,* time of aortic cannulation.

During rewarming, and before separation from cardiopulmonary bypass, the N20-P22 complex after stimulation of the left ulnar nerve again disappeared for a period of 20 minutes before gradual recovery of the SEP toward baseline (Fig. 2, *B*).

No significant changes according to our a priori criteria were observed in the SEPs of the two patients who had mild postoperative brachial plexopathies.

Criterion analysis. Fig. 3, *A* to *F* illustrates each measurement of the six SEP parameters discussed earlier in each normal patient and each patient who had an intraoperative stroke. A linear discriminant analysis confirms the qualitative impression given in these graphs that none of the latency-based parameters (Fig. 3, *C* to *F*) were able to discriminate between the patients in the two groups. However, Fig. 3, *A* and *B* indicates that the amplitude asymmetry and the amplitude variability measures could be useful in classifying patients. To test these hypotheses, linear discriminant analyses in which the maximum value of the amplitude asymmetry and amplitude variability for each patient were tested separately for their ability to classify patients. A significant classification based on the amplitude asymmetry was achieved (Wilks lambda = 0.231, $p < 0.001$). All patients with any amplitude asymmetry measurement greater than 17.1 were correctly classified as having intraoperative strokes. Other patients did not have intraoperative strokes. Significant classification was also possible using the amplitude variability (Wilks lambda = 0.414, $p < .001$), but as can be seen in Fig. 3, *B*, the distinction is less than for the amplitude asymmetry. In fact, linear discriminant analysis determined a threshold of 21.7 for the amplitude variability. This correctly classified all patients with stroke but misclassified one patient without a stroke as being in the stroke category.

Temperature effects. The temperature dependency of the SEP has been widely recognized[18, 19] and can complicate the interpretation of the SEP during cardiac operations in which hypothermia is deliberately used. Therefore the relationship between nasopharyngeal temperature and the SEP latencies and amplitudes was studied in the group of neurologically intact subjects. Linear regression analysis indicated a significant effect of temperature on the latency of the Erb point, N20, and P22 potentials. Statistically significant ($p < 0.001$) slopes (mean ± standard deviation) for the variation in the Erb's point latency (−0.4 msec/° C ± 0.02), the N20 latency (−1.0 msec/° C ± 0.02), and the P22 latency (−1.2 msec/° C ± 0.03) versus temperature, respectively. These values were similar to but somewhat smaller than the slopes reported by Markand and associates.[18, 19] The effect of nasopharyngeal temperature on the amplitude of N20-P22 complex was much less significant and amounted only to 0.03 μV/° C.

No significant correlations ($R = -0.02, p > 0.5$) were detected between the nasopharyngeal temperature and the amplitude asymmetry although there was a significant correlation between the amplitude variability and temperature ($R = -0.15, p < 0.001$). Despite the fact that latency differences show less variability with temperature than the raw latencies, there was a significant effect of temperature on the latency asymmetry values as well.

Effect of stimulus current. Qualitative observations on eight patients indicated that the asymmetry of the evoked responses increased with decreasing stimulus intensity. To determine the effect of stimulus current on the amplitude asymmetry in the 21 "normal" patients, we plotted the mean value of the amplitude asymmetry as a function of the intensity of the somatosensory stimulus (Fig. 4). From this figure it is clear that the asymmetry increased as the stimulus current decreased until the amplitude of the stimulus was so small (4 mA) that the response could not be distinguished from baseline noise. At this point, the amplitude asymmetry decreased because noise levels are symmetric.

Discussion

Ability to detect intraoperative stroke. In this small study somatosensory evoked responses were able to identify in real time which patients had an intraoperative stroke, localize the area of ischemia,

Fig. 3. Summary of SEP measurements in the group of patients with normal results of preoperative and postoperative examinations and those with intraoperative strokes. From each of the 1768 SEP recordings made, all available measurements for each variable are plotted using a separate column for each patient. Data for each variable are shown on separate plots: **A,** Amplitude asymmetry; **B,** amplitude variability; **C,** P22 latency asymmetry; **D,** N20 latency asymmetry; **E,** N13 latency asymmetry; **F,** Erb point latency asymmetry.

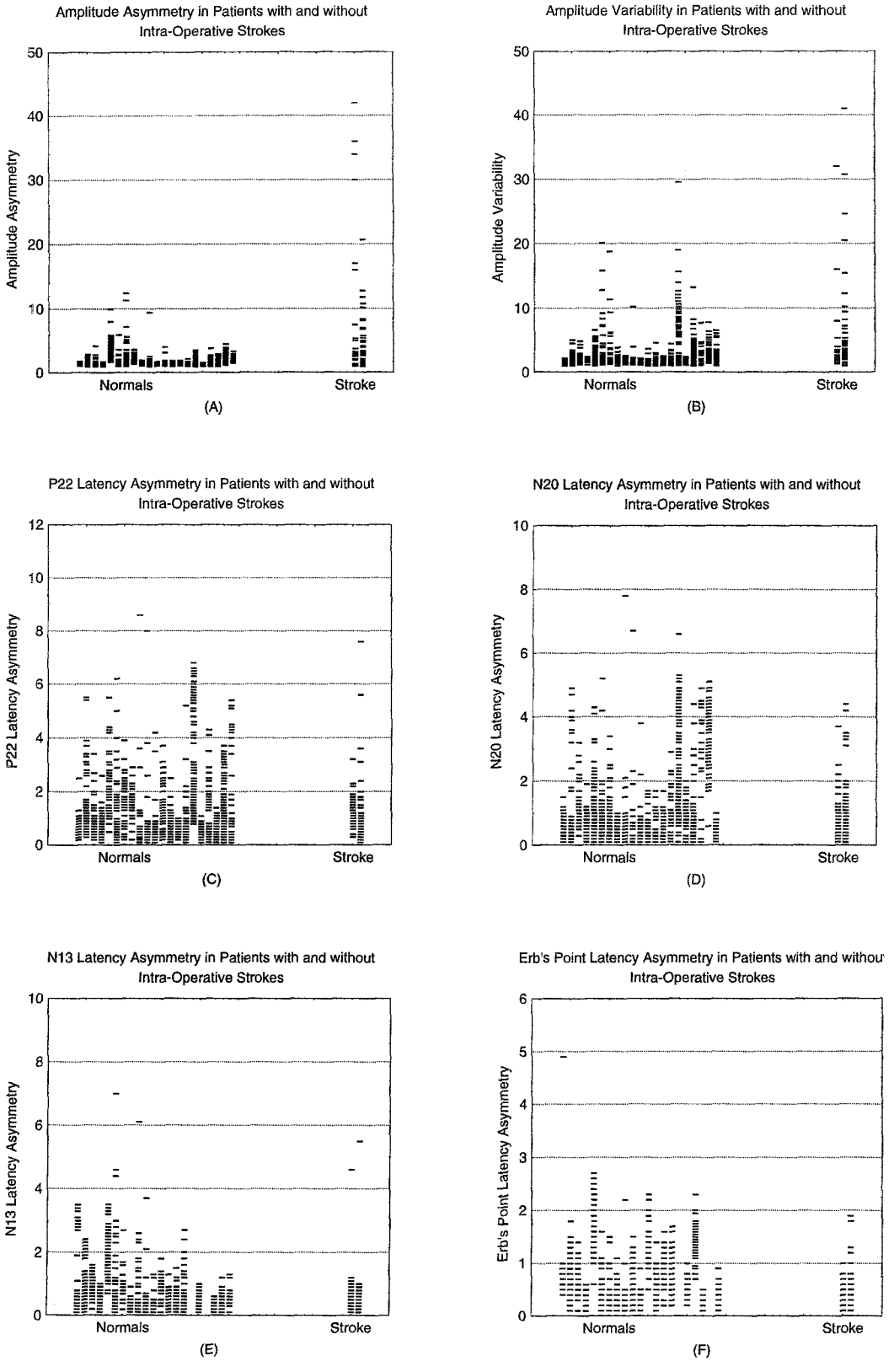

Fig. 3. For legend see opposite page.

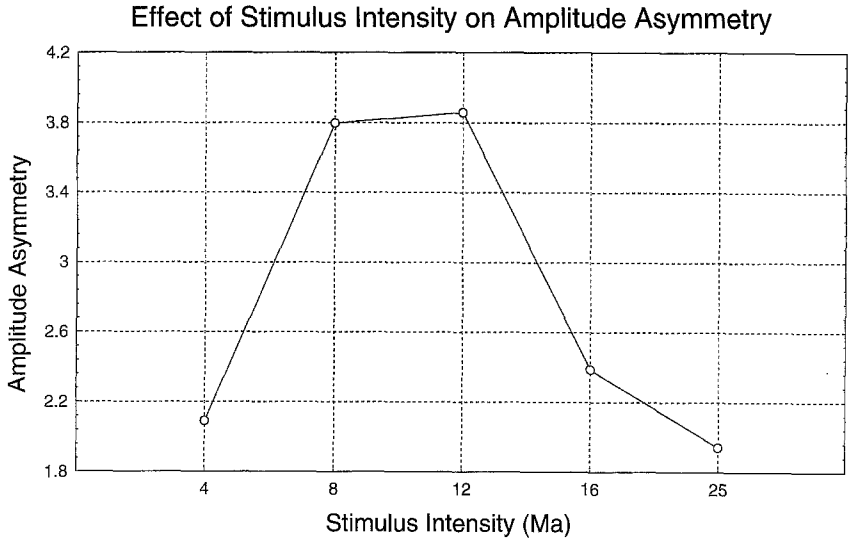

Fig. 4. The effects of the stimulation current on the amplitude asymmetry for the 21 patients with normal results of preoperative and postoperative neurologic examinations. The amplitude asymmetry is smaller at 25 mA stimulus currents than with 8, 12, or 16 mA stimulus currents. The small amplitude asymmetry values at stimulation currents less than 8 mA is the result of the fact that, for such low-amplitude stimuli, the amplitude of the evoked response has fallen below the level of background noise.

and determine the time at which the event occurred during the operation. Crucial to this ability are the criteria used to determine which changes in the SEP indicate cerebral ischemia. Although the a priori criterion of total, unilateral disappearance of a wave or set of waves was effective in this small group of patients, in larger groups of patients the application of this conservative criterion may well lead to false negative results. A detailed analysis of the amplitude asymmetry, the amplitude variability, and the latency asymmetry derived from the SEP data provided insight into how well these parameters could be used to distinguish the "normal" patients from the group of patients with intraoperative stroke. This analysis demonstrated that latency-based criteria were not very useful in distinguishing the patients who had intraoperative strokes. However, finding amplitude asymmetry values greater than 17 on any measurement correlated with the occurrence of intraoperative stroke. In addition, the amplitude asymmetry was independent of temperature, rendering it an important parameter for predicting intraoperative cerebral ischemia during operations involving deliberate hypothermia.

One problem inherent in using SEP amplitude asymmetry as a criterion for cerebral injury is that it is strongly biased toward detecting unilateral or asymmetric central nervous system lesions. To overcome this problem, we studied the amplitude variability. As Fig. 3, *B* indicates, amplitude variability measurements greater than 21 during an operation indicated a high probability of intraoperative stroke, although this criterion lead to false positive results. This implies that a persistent, bilateral decrease in the amplitude of more than a factor of 21 from baseline could be an indicator of bilateral cerebral ischemia. However, further study is required to validate the use of bilateral decreases in SEP amplitude alone to diagnose cerebral ischemia, because it is widely known that bilateral decreases in cortical SEP amplitudes may be observed, even in the absence of cerebral ischemia, during deep hypothermia or at high inspired concentrations of halogenated anesthetics.[13] This is consistent with our observation the amplitude variability, unlike the amplitude asymmetry measure, has a strong temperature dependence.

We do *not* suggest that the criteria we have described for detecting stroke using the SEP will work in all cases, and we cannot give a true estimate of the actual sensitivity and specificity of this test given the small number of patients and the large potential variation between patients with intraoperative strokes. Such an estimate will require additional studies with larger numbers of patients. However, the current work greatly constrains the

decision criteria that would be useful in detecting intraoperative stroke. The commonly used rule that a 50% decrease in evoked potential amplitude suggests a neurologic injury is too conservative when applied to patients undergoing cardiac operations, because substantial changes in temperature and anesthesia occur during these procedures. We have demonstrated that it is not uncommon to see 90% decreases in amplitude in patients without strokes.

Another potential problem with the criteria for cerebral ischemia established by this study is that they were derived from SEP measurements obtained throughout the operation without specifically accounting for the many physiologic changes occurring at various times during the operation. For example, the greatest variability in SEP amplitude, latency, and amplitude asymmetry among the patients without neurologic deficits were observed during the periods of active cooling and rewarming (Fig. 2, *A*). Future studies directed at examining the probability distributions of our parameters as functions of temperature and time during the operation will increase the sensitivity of detecting central nervous system injury using SEP monitoring. It is important to note that our criteria for detecting cerebral ischemia by SEP were based on the clinical outcome measure of stroke. The present study was *not* designed to detect more subtle neuropsychologic abnormalities.

No significant changes in SEP amplitudes or latencies were observed in the two patients in whom mild brachial plexopathies developed. This finding contrasts with the reports of Hickey,[16] Jellish,[15] and their associates that brachial plexus injuries can be detected intraoperatively by SEP monitoring. A plausible explanation for this discrepancy is that since the plexopathies that occurred in the two patients in our study were subtle and detected only on detailed neurologic examination, the injury may not have been sufficiently severe to change the SEPs. An alternative explanation is that the criteria we applied to define a significant change in the SEP were not sensitive enough to detect mild peripheral neuropathies. Support for this hypothesis comes from the fact that Hickey and coworkers[16] regarded changes in SEP amplitude as little as 60% and latency changes of only 7% to 9% as indicative of plexopathy. In the current study, variability of SEP amplitudes and latencies observed in the group of "normal" patients was much greater than this.

Certain technical factors, such as the placement of the stimulating and recording electrodes and the intensity of the somatosensory stimulus, may contribute to an amplitude asymmetry in the absence of cerebral ischemia, as indicated in Fig. 4. Thus great care in positioning electrodes and the use of a stimulation currents of at least 25 mA with 0.5 msec duration would be recommended to minimize this technical contribution to the amplitude asymmetry.

Anatomic specificity. SEP monitoring has not been routinely applied for the intraoperative assessment of central nervous system function during cardiac operations because of the belief that SEPs may be insensitive for detecting neurologic injury outside the somatosensory system. Our demonstration of significant changes in the intraoperative cortical SEP waveforms in two patients with stroke despite no (patient 16) or minor (patient 20) postoperative sensory deficits suggests that SEP monitoring may be applicable for detecting some ischemic lesions outside the somatosensory system proper. One explanation can be found in the concept of an ischemic penumbra. Regional decreases in cerebral blood flow produce an area of maximum ischemia surrounded by a larger ischemic penumbra. At critical levels of blood flow, infarction occurs within the region of maximum ischemia, whereas neuronal function in the ischemic penumbra may exhibit only transient dysfunction followed by recovery during reperfusion. If any portion of the somatosensory pathway lies within the ischemic penumbra, changes will occur in the SEP waveform. The observation that maximum changes in the cortical SEP waveforms were detected at the time of injury and were followed by a gradual recovery was consistent with this concept. In addition, another less well-defined mechanism known as diaschisis[22] could explain the production of SEP abnormalities as a consequence of injuries outside the somatosensory pathways. Diaschisis describes the decrease in neuronal activity in brain regions remote from the site of injury because of the reduction in neuronal activity at the site of injury.

Mechanism and timing of stroke. Stroke occurred in one patient (patient 16) during removal of the aortic crossclamp and in another (patient 20) during the initiation of cardiopulmonary bypass (see Figs. 1 and 2, *B*). These events likely reflect embolic infarctions because of the sudden onset of changes on the SEPs. This is consistent with the findings of Clark and colleagues,[4] which suggested that the maximum number of emboli occurred at the time of aortic cannulation and around the time of removal of the aortic crossclamp.

Criteria based on changes in cortical SEP amplitude and symmetry were useful in detecting intraoperative cerebral ischemia during cardiac operations. In addition, SEP monitoring also provides a valuable insight into the pathophysiology of neurologic complications of cardiac operations.

We thank Dr. L. H. Edmunds and Dr. Michael Acker from the Department of Cardiothoracic Surgery and Dr. Timothy Conahan, Dr. Karen Traber, Dr. C. William Hanson III, and Dr. Warren Levy from the Department of Anesthesia for their cooperation during this study.

REFERENCES

1. Mills SA. Cerebral injury and cardiac operations. Ann Thorac Surg 1993;56:S86-91.
2. Shaw PJ, Bates D, Cartlidge NEF, et al. Long-term intellectual dysfunction following coronary artery bypass graft surgery: a six-month follow-up study. Q J Med 1987;239:259-68.
3. Townes BD, Bashein G, Horbein TF, et al. Neurobehavioral outcomes in cardiac operations. J Thorac Cardiovasc Surg 1989;98:774-82.
4. Clark RE, Brillman J, Davis DA, et al. Microemboli during coronary artery bypass grafting. J Thorac Cardiovasc Surg 1995;109:249-58.
5. Grosset DG, Georgiadis D, Stirling S, et al. Subclinical embolism in patients undergoing cardiac valve implantation and coronary artery bypass surgery. Eur J Cardiothorac Surg 1994;8:63-6.
6. Taylor KM, Devlin BJ, Mittra SM, et al. Assessment of cerebral damage during open-heart surgery: a new experimental model. Scand J Thorac Cardiovasc Surg 1980;14:197-203.
7. Aberg T, Tyden H, Ronquist G, et al. Release of adenylate kinase into cerebrospinal fluid during open-heart surgery and its relation to postoperative intellectual function. Lancet 1982:1139-42.
8. Schell RM, Kern FH, Reves JG. The role of continuous jugular venous saturation monitoring during cardiac surgery with cardiopulmonary bypass. Anesth Analg 1992;74:627-9.
9. Arom KV, Cohen DE, Strobl FT. Effect of intraoperative intervention on neurological outcome based on electroencephalographic monitoring during cardiopulmonary bypass. Ann Thorac Surg 1989;48:476-83.
10. Edmonds HL Jr, Griffiths LK, van der Laken J, Slater AD, Shields CB. Quantitative electroencephalographic monitoring during myocardial revascularization predicts postoperative disorientation and improves outcome. J Thorac Cardiovasc Surg 1992;103:555-63.
11. Bashein G, Nessly ML, Bledsoe SW, et al. Electroencephalography during surgery with cardiopulmonary bypass and hypothermia. Anesthesiology 1992;76:878-91.
12. Levy WJ. Monitoring of the electroencephalogram during cardiopulmonary bypass. Anesthesiology 1992;76:876-7.
13. Coles JG, Taylor MJ, Pearce JM, et al. Cerebral monitoring of somatosensory evoked potentials during profoundly hypothermic circulatory arrest. Circulation 1984;70(Suppl):I96-102.
14. Aren C, Badr G, Feddersen K, et al. Somatosensory evoked potentials and cerebral metabolism during cardiopulmonary bypass with special reference to hypotension induced by prostacyclin infusion. J Thorac Cardiovasc Surg 1985;90:73-9.
15. Jellish WS, Martucci J, Blakeman B, et al. Somatosensory evoked potential monitoring of the brachial plexus to predict nerve injury during internal mammary artery harvest: intraoperative comparisons of the Rultract and Pittman sternal retractors. J Cardiothorac Vasc Anesth 1994;8:398-403.
16. Hickey C, Gugino LD, Agilo LS, et al. Intra-operative somatosensory evoked potential monitoring predicts peripheral nerve injury during cardiac surgery. Anesthesiology 1993;78:29-35.
17. Fava E, Bortolani E, Ducati A, et al. Role of SEP in identifying patients requiring temporary shunt during carotid endarterectomy. Electroencephalogr Clin Neurophysiol 1992;84:426-32.
18. Markand ON, Warren C, Mallik G, et al. Effects of hypothermia on short latency somatosensory evoked potentials in humans. Electroencephalogr Clin Neurophysiol 1990;77:416-24.
19. Markand ON, Warren C, Mallik GS, et al. Temperature-dependent hysteresis in somatosensory and auditory evoked potentials. Electroencephalogr Clin Neurophysiol 1990;77:425-35.
20. American EEG Society guidelines on evoked potentials. J Clin Neurophysiol 1994;11:66-70.
21. Cheung AT, Savino JS, Weiss SJ, et al. Detection of acute embolic stroke during mitral valve replacement using somatosensory evoked potential monitoring. Anesthesiology 1995;83:208-10.
22. Feeny DM, Baron JC. Diaschisis. Stroke 1986;17:817-30.